Add a1

WE CLAIM:

1. A method of treating a patient with diabetes mellitus, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a donor; and

(b) transferring the stem cell into the patient, wherein the stem cell differentiates into an insulin-producing cell,

wherein the patient does not serve as the donor for said stem cells of step a.

2. The method of claim 1, wherein the patient is a human and the donor for said stem cells of step a is a non-human mammal.

3. The method of claim 1 or 2, wherein the patient is not treated with an immunosuppressive agent prior to step (b).

4. The method of claim 1 wherein, prior to the step of transferring, the stem cell is treated *ex vivo* with an agent selected from the group consisting of EGF, bFGF-2, high glucose, KGF, HGF/SF, GLP-1, exendin-4, IDX-1, a nucleic acid molecule encoding IDX-1, betacellulin, activin A, TGF-β, and combinations thereof.

5. The method of claim 1, wherein the step of transferring is performed via endoscopic retrograde injection.

6. The method of claim 1 additionally comprising the step of:

(c) treating the patient with an immunosuppressive agent.

7. The method of claim 6 wherein said immunosuppressive agent prevents an

immune response.

8. The method of claim 6 wherein said immunosuppressive agent delays the occurrence of an immune response.

9. The method of claim 6 wherein said immunosuppressive agent decreases the intensity of an immune response.

10. The method of claim 6, 7, 8 or 9 wherein the immune response is transplant rejection.

11. The method of claim 6, wherein the immunosuppressive agent is selected from the group consisting of FK-506, cyclosporin, and GAD65 antibodies.

12. A method of treating a patient with diabetes mellitus, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a donor;

(b) culturing the stem cell *ex vivo*; and

(c) transferring the progenitor cell into the patient, wherein the progenitor cell differentiates into an insulin-producing beta cell,

wherein the patient does not serve as the donor for said stem cells of step a.

13. A method of treating a patient with diabetes mellitus, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a donor;

(b) expanding the stem cell *ex vivo* to produce a progenitor cell; and

(c) transferring the progenitor cell into the patient, wherein the progenitor cell differentiates into an insulin-producing beta cell,

wherein the patient does not serve as the donor for said stem cells of step a.

14. The method of claim 12 or 13, wherein the patient is a human and the donor for said stem cells of step a is a non-human mammal.

15. The method of claim 12 or 13, wherein the patient is not treated with an immunosuppressive agent prior to step (b).

16. The method of claim 13, wherein the step of expanding is performed in the presence of an agent selected from the group consisting of EGF, bFGF-2, high glucose, KGF, HGF/SF, GLP-1, exendin-4, IDX-1, a nucleic acid molecule encoding IDX-1, betacellulin, activin A, TGF-β, and combinations thereof.

17. The method of claim 12 or 13, wherein the step of transferring is performed via endoscopic retrograde injection.

18. The method of claim 12 additionally comprising the step of:
(d) treating the patient with an immunosuppressive agent.

19. The method of claim 13 additionally comprising the step of:
(d) treating the patient with an immunosuppressive agent.

20. The method of claim 18 or 19 wherein said immunosuppressive agent prevents an immune response.

21. The method of claim 18 or 19 wherein said immunosuppressive agent delays

the occurrence of an immune response.

22. The method of claim 18 or 19 wherein said immunosuppressive agent decreases the intensity of an immune response.

23. The method of claim 18, 19, 20, 21 or 22, wherein said immune response is transplant rejection.

24. The method of claim 18 or 19, wherein the immunosuppressive agent is selected from the group consisting of FK-506, cyclosporin, and GAD65 antibodies.

25. A method of treating a patient with diabetes mellitus, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a donor;

(b) expanding the stem cell to produce a progenitor cell;

(c) differentiating the progenitor cell in culture to form pseudo-islet like aggregates; and

(d) transferring the pseudo-islet like aggregates into the patient,

wherein the patient does not serve as the donor for said stem cells of step a.

26. The method of claim 25, wherein the patient is a human and the donor for said stem cells of step a is a non-human mammal.

27. The method of claim 25 or 26, wherein the patient is not treated with an immunosuppressive agent prior to step (b).

28. The method of claim 25, wherein the step of expanding is performed in the presence of an agent selected from the group consisting of EGF, bFGF-2, high glucose, KGF, HGF/SF, GLP-1, exendin-4, IDX-1, a nucleic acid molecule encoding IDX-1, betacellulin, activin A, TGF-β, and combinations thereof.

29. The method of claim 25, wherein the step of transferring is performed via endoscopic retrograde injection.

30. The method of claim 25 additionally comprising the step of:

(e) treating the patient with an immunosuppressive agent.

31. The method of claim 30 wherein said immunosuppressive agent prevents an immune response.

32. The method of claim 30 wherein said immunosuppressive agent delays the occurrence of an immune response.

33. The method of claim 30 wherein said immunosuppressive agent decreases the intensity of an immune response.

34. The method of claim 30, 31, 32 or 33 wherein the immune response is transplant rejection.

35. The method of claim 30, wherein the immunosuppressive agent is selected from the group consisting of FK-506, cyclosporin, and GAD65 antibodies.

36. A method of transplanting into a mammal, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a

donor; and

(b) transferring the stem cell into the mammal, wherein the stem cell differentiates into an insulin-producing cell.

37. The method of claim 36, wherein the mammal serves as the donor for said stem cells of step a.

38. The method of claim 36, wherein the mammal does not serve as the donor for said stem cells of step a.

39. The method of claim 36, wherein the mammal is a human and the donor for said stem cells of step a is a non-human mammal.

40. The method of claim 38 or 39, wherein the mammal is not treated with an immunosuppressive agent prior to step (b).

41. The method of claim 36 wherein, prior to the step of transferring, the stem cell is treated *ex vivo* with an agent selected from the group consisting of EGF, bFGF-2, high glucose, KGF, HGF/SF, GLP-1, exendin-4, IDX-1, a nucleic acid molecule encoding IDX-1, betacellulin, activin A, TGF-β, and combinations thereof.

42. The method of claim 36, wherein the step of transferring is performed via endoscopic retrograde injection.

43. The method of claim 36 additionally comprising the step of:

(c) treating the mammal with an immunosuppressive agent.

44. The method of claim 43 wherein said immunosuppressive agent prevents an immune response.

45. The method of claim 43 wherein said immunosuppressive agent delays the occurrence of an immune response.

46. The method of claim 43 wherein said immunosuppressive agent decreases the intensity of an immune response.

47. The method of claim 44, 45 or 46 wherein the immune response is transplant rejection.

48. The method of claim 43, wherein the immunosuppressive agent is selected from the group consisting of FK-506, cyclosporin, and GAD65 antibodies.

49. A method of transplanting into a mammal, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a donor;

(b) culturing the stem cell *ex vivo*; and

(c) transferring the progenitor cell into the mammal, wherein the progenitor cell differentiates into an insulin-producing beta cell.

50. A method of transplanting into a mammal, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a donor;

(b) expanding the stem cell *ex vivo* to produce a progenitor cell; and

(c) transferring the progenitor cell into the mammal, wherein the progenitor cell differentiates into an insulin-producing beta cell.

51. The method of claim 49 or 50, wherein the mammal serves as the donor for said stem cells of step a.

52. The method of claim 49 or 50, wherein the mammal does not serve as the donor for said stem cells of step a.

53. The method of claim 49 or 50, wherein the mammal is a human and the donor for said stem cells of step a is a non-human mammal.

54. The method of claim 52 or 53, wherein the mammal is not treated with an immunosuppressive agent prior to step (b).

55. The method of claim 50, wherein the step of expanding is performed in the presence of an agent selected from the group consisting of EGF, bFGF-2, high glucose, KGF, HGF/SF, GLP-1, exendin-4, IDX-1, a nucleic acid molecule encoding IDX-1, betacellulin, activin A, TGF-β, and combinations thereof.

56. The method of claim 49 or 50, wherein the step of transferring is performed via endoscopic retrograde injection.

57. The method of claim 49 additionally comprising the step of:
(d) treating the mammal with an immunosuppressive agent.

58. The method of claim 50 additionally comprising the step of:
(d) treating the mammal with an immunosuppressive agent.

59. The method of claim 57 wherein said immunosuppressive agent prevents an

immune response.

60. The method of claim 57 wherein said immunosuppressive agent delays the occurrence of an immune response.

61. The method of claim 57 wherein said immunosuppressive agent decreases the intensity of an immune response.

62. The method of claim 58 wherein said immunosuppressive agent prevents an immune response.

63. The method of claim 58 wherein said immunosuppressive agent delays the occurrence of an immune response.

64. The method of claim 58 wherein said immunosuppressive agent decreases the intensity of an immune response.

65. The method of claim 59, 60, 61, 62, 63 or 64 wherein said immune response is transplant rejection.

66. The method of claim 57 or 58, wherein the immunosuppressive agent is selected from the group consisting of FK-506, cyclosporin, and GAD65 antibodies.

67. A method of transplanting into a mammal, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a donor;

(b) expanding the stem cell to produce a progenitor cell;

(c) differentiating the progenitor cell in culture to form pseudo-islet like aggregates; and

(d) transferring the pseudo-islet like aggregates into the mammal.

68. The method of claim 67, wherein the mammal serves as the donor for said stem cells of step a.

69. The method of claim 67, wherein the mammal does not serve as the donor for said stem cells of step a.

70. The method of claim 67, wherein the mammal is a human and the donor for said stem cells of step a is a non-human mammal.

71. The method of claim 69 or 70, wherein the mammal is not treated with an immunosuppressive agent prior to step (b).

72. The method of claim 67, wherein the step of expanding is performed in the presence of an agent selected from the group consisting of EGF, bFGF-2, high glucose, KGF, HGF/SF, GLP-1, exendin-4, IDX-1, a nucleic acid molecule encoding IDX-1, betacellulin, activin A, TGF-β, and combinations thereof.

73. The method of claim 67, wherein the step of transferring is performed via endoscopic retrograde injection.

74. The method of claim 67 additionally comprising the step of:

(e) treating the mammal with an immunosuppressive agent.

75. The method of claim 74 wherein said immunosuppressive agent prevents an

immune response.

76. The method of claim 74 wherein said immunosuppressive agent delays the occurrence of an immune response.

77. The method of claim 74 wherein said immunosuppressive agent decreases the intensity of an immune response.

78. The method of claim 75, 76 or 77 wherein the immune response is transplant rejection.

79. The method of claim 74, wherein the immunosuppressive agent is selected from the group consisting of FK-506, cyclosporin, and GAD65 antibodies.

80. A transplant graft comprising an isolated, nestin-positive human pancreatic stem cell that is not a neural stem cell.

81. The transplant graft of claim 80 wherein said stem cell is immunoprivileged.

82. The transplant graft of claim 80 wherein said stem cell does not express class I MHC antigens.

83. The transplant graft of claim 80 wherein said stem cell does not express class II MHC antigens.

84. The transplant graft of claim 80 wherein said stem cell does not express class I or class II MHC antigens.

85. A method of treating a patient with liver disease, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a donor; and

(b) transferring the stem cell into the patient, wherein the stem cell differentiates into a hepatocyte, wherein the patient does not serve as the donor for said stem cells of step a.

86. A method of treating a patient with liver disease, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a donor;

(b) expanding the stem cell *ex vivo* to produce a progenitor cell; and

(c) transferring the progenitor cell into the patient, wherein the progenitor cell differentiates into a hepatocyte,

wherein the patient does not serve as the donor for said stem cells of step a.

87. A method of treating a patient with liver disease, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a donor;

(b) differentiating the stem cell *ex vivo* to produce a hepatocyte; and

(c) transferring the hepatocyte into the patient,

wherein the patient does not serve as the donor for said stem cells of step a.

88. The method of claim 85, 86 or 87, wherein the patient is a human and the donor for said stem cells of step a is a non-human mammal.

89. The method of claim 85, 86, or 87, wherein the patient is not treated with an immunosuppressive agent prior to step (b).

90. The method of claim 88, wherein the patient is not treated with an immunosuppressive agent prior to step (b).

91. The method of claim 85, 86 or 87 additionally comprising the step of:

(c) treating the patient with an immunosuppressive agent.

92. The method of claim 87 additionally comprising the step of:

(c) treating the patient with an immunosuppressive agent.

93. The method of claim 91 wherein said immunosuppressive agent prevents an immune response.

94. The method of claim 91 wherein said immunosuppressive agent delays the occurrence of an immune response.

95. The method of claim 91 wherein said immunosuppressive agent decreases the intensity of an immune response.

96. The method of claim 93 wherein the immune response is transplant rejection.

97. The method of claim 94 wherein the immune response is transplant rejection.

98. The method of claim 95 wherein the immune response is transplant rejection.

99. The method of claim 96 wherein the immune response is transplant rejection.

100. A method of transplanting into a mammal, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a

donor; and

(b) transferring the stem cell into said mammal, wherein the stem cell differentiates into a hepatocyte.

101. The method of claim 100, wherein said mammal serves as the donor for said stem cells of step a.

102. A method of transplanting into a mammal, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a donor;

(b) expanding the stem cell *ex vivo* to produce a progenitor cell; and

(c) transferring the progenitor cell into said mammal, wherein the progenitor cell differentiates into a hepatocyte.

103. The method of claim 102, wherein said mammal serves as the donor for said stem cells of step a.

104. A method of transplanting into a mammal, comprising the steps of:

(a) isolating a nestin-positive pancreatic stem cell from a pancreatic islet of a donor;

(b) differentiating the stem cell *ex vivo* to produce a hepatocyte; and

(c) transferring the hepatocyte into said mammal.

105. The method of claim 104, wherein said mammal serves as the donor for said stem cells of step a.

106. The method of claim 100, 102 or 104, wherein said mammal does not serve as the donor for said stem cells of step a.

107. The method of claim 100, 102 or 104, wherein said mammal is a human and the donor for said stem cells of step a is a non-human mammal.

108. The method of claim 106, wherein said mammal is not treated with an immunosuppressive agent prior to step (b).

109. The method of claim 107, wherein said mammal is not treated with an immunosuppressive agent prior to step (b).

110. The method of claim 106 additionally comprising the step of:

(c) treating said mammal with an immunosuppressive agent.

111. The method of claim 107 additionally comprising the step of:

(c) treating said mammal with an immunosuppressive agent.

112. The method of claim 110 wherein said immunosuppressive agent prevents an immune response.

113. The method of claim 110 wherein said immunosuppressive agent delays the occurrence of an immune response.

114. The method of claim 110 wherein said immunosuppressive agent decreases the intensity of an immune response.

115. The method of claim 112 wherein the immune response is transplant rejection.

116. The method of claim 113 wherein the immune response is transplant rejection.

117. The method of claim 114 wherein the immune response is transplant rejection.

118. A transplant graft comprising an isolated, nestin-positive human liver stem cell that is not a neural stem cell.

119. The transplant graft of claim 118 wherein said stem cell is immunoprivileged.

120. The transplant graft of claim 118 wherein said stem cell does not express class I MHC antigens.

121. The transplant graft of claim 118 wherein said stem cell does not express class II MHC antigens.

122. The transplant graft of claim 118 wherein said stem cell does not express class I or class II MHC antigens.

123. A transplant graft comprising an isolated, nestin-positive human stem cell that is not a neural stem cell, that is capable of transplant into an animal without causing graft versus host rejection.

124. The transplant graft of claim 123 wherein said stem cell is not major histocompatibility complex class I or class II restricted.

125. A pharmaceutical composition comprising the transplant graft of claim 80 admixed with a physiologically compatible carrier.

126. A pharmaceutical composition comprising the transplant graft of claim 118 admixed with a physiologically compatible carrier.

127. A pharmaceutical composition comprising the transplant graft of claim 123 admixed with a physiologically compatible carrier.